# Pharmacotherapy for Substance Use Disorders

Jodie Anne Trafton, Ph.D.

# Substitution Therapies

- Concept:  Patients are given a long-acting, slowly absorbed version of their drug of choice (DOC).  This prevents withdrawal symptoms, reduces cravings, and by occupying a large percentage of receptors, stops the high (and other effects) of the DOC.

# Examples

- Opioid Substitution Therapy (AKA opioid (methadone) maintenance, opioid agonist therapy)
  - Methadone – a long acting synthetic mu opioid, also acts as a weak NMDA receptor antagonist, which may reduce development of tolerance.
  - LAAM – a long acting synthetic mu opioid whose metabolites are also active mu opioids.
  - Buprenorphine – a long acting partial agonist at the mu opioid receptor (prevents overdosing), also a kappa opioid receptor antagonist (reduces dysphoria associated with withdrawal)

# More examples:

- Nicotine Replacement  Therapy
  - Nicotine Patch
  - Nicotine Gum

# Drug Antagonists

- Naltrexone for Opioid Addiction
  - Concept: Naltrexone blocks the effects of opioids on their receptors. If given to detoxified opioid addicts, it will completely prevent the effects of opioids if they are taken.
  - Medication adherence is a problem.
- Cocaine Vaccine
  - Concept: Patients are innoculated with cocaine linked to a protein, triggering an immune response and antibody production against cocaine. These antibodies bind cocaine in the blood, preventing it from reaching transporters in the brain and reducing its effects.
  - This therapy is currently not available.

# Reward Antagonists

- Naltrexone for Alcohol Use Disorder
  - Concept:  By blocking the effects of opioids released in the nucleus accumbens, naltrexone prevents the dopamine release and nucleus accumbens activation normally produced by alcohol consumption.  All other effects of alcohol still occur.  By reducing the reward associated with alcohol use, extinction of alcohol seeking behaviors can occur, alcohol-primed alcohol consumption is reduced (less binge drinking), and craving is reduced.

# Anti-craving medication

- Acamprosate
  - A pharmacologically messy drug that has effects on glutamatergic systems. Seems to reduce alcohol craving via an as yet undetermined mechanism
  - Only available in Europe

# Aversive Agents

- Disulfiram
  - Concept:  Alcohol is broken down first to acetaldehyde, a compound that causes a diverse array of severely unpleasant and potentially dangerous symptoms.  Disulfiram inhibits the enzyme that breaks down acetaldehyde, thus resulting in acetaldehyde build-up following alcohol consumption.  To avoid feeling sick, people on disulfiram will avoid drinking.
  - Compliance is low and treatment is potentially dangerous if the patient does not have control over their drinking.
  - Might be useful in preventing addiction.

# Drug Mimics

- Topiramate for Alcohol Use Disorder
  - Concept:  A GABA-A receptor agonist. This drug will activate the main target of alcohol, thus potentiating alcohol's effects.  Thus, a patient will have to drink less alcohol to get intoxicated and will reduce their drinking.
  - Maybe helpful for people who can't stop drinking and are having alcohol toxicity problems (e.g. liver or brain damage), but kind of a strange therapy in my opinion.

# Drugs that reduce Withdrawal Symptoms

- Benzodiazepines for Alcohol withdrawal
- Methadone/Buprenorphine for opioid withdrawal
- Alpha2-adrenergic receptor agonists – reduce activation of the locus cerruleus. Reduces anxiety and agitation during withdrawal.
  - Clonidine/Lofexidine